How Interpersonal Psychotherapy Changes the Brain: A Study of fMRI in Borderline Personality Disorder

How interpersonal psychotherapy changes the brain: a fMRI study in borderline personality disorder

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Abstract

Background

Recent guidelines and systematic reviews suggested that disorder-specific psychotherapeutic interventions are first-line treatments for borderline personality disorder. This study is aimed to evaluate changes of brain activity in BPD patients (DSM-5) who received interpersonal psychotherapy adapted to BPD-revised (IPT-BPD-R) in comparison with patients who were in waiting list (WL).

Methods

Forty-three subjects with a BPD diagnosis (DSM-5) were randomly assigned to IPT-BPD-R (N = 22 patients) or waiting list with clinical management (N = 21 patients) for 10 months. Both groups were tested before and after treatment with the CGI-S, the BPDSI, the BIS-11, and the Autobiographical Interview. Both groups underwent a pre-treatment fMRI run and a post-treatment fMRI run. fMRI task consisted of presentation of resolved and unresolved life events compared with a neutral condition. We analyzed all structural and functional images using Statistical Parametric Mapping 12 software interfaced on Matlab. Clinical data were analyzed with the ANOVA for repeated measures. Patients were recruited from September 2017 and April 2019.

Results

Clinical results: significant between-subjects effect was found for the four rating scales in favor of the IPT-BPD-R treated group (CGI-S: P = 0.009; BPDSI: P = 0.01; BIS-11: P = 0.031; SOFAS: P = 0.02).

fMRI results: Post versus Pre for the contrast unresolved life event condition versus neutral condition showed a significantly decreased activity of the right Temporal Parietal Junction (rTPJ, x = 45, y = -51, z = 36) (P = 0.043) and of the right Anterior Cingulate Cortex (rACC, x = -4, y = 37, z = 8) (P = 0.021).

Conclusions: IPT-BPD-R appears to be effective in treating BPD symptoms and these clinical effects are reflected in functional changes observed with fMRI. Brain areas that showed a

modulation in their activity are TPJ and ACC, that are involved in mentalization processes fundamental in BPD pathology. The trial was registered in the Australian New Zealand Clinical Trials Registry (ANZCTR) and allocated the code: ACTRN12619000078156.

Key-words: functional magnetic resonance imaging; borderline personality disorder, interpersonal psychotherapy for borderline personality disorder revised; waiting list; autobiographical memories; brain activity; temporo-parietal junction; anterior cingulate cortex.

1. Introduction

Borderline personality disorder (BPD) is a complex personality disorders, accounting for 6.4% in primary care, 10% of all psychiatric outpatients, and around 20% of inpatients (1,2). It is a severe and heterogeneous psychiatric disorder mainly characterized by dysregulated affectivity, scarce impulse control, disturbed interpersonal relationships, and diffused identity (3,4). Treatment of this complex disorder has always been an arduous challenge and there are still outstanding and debated issues among clinicians and researchers. Deficit in regulating internal and external states that is one of the consequences of the lack of identity integration partially respond to pharmacological treatments and more often benefit from a psychotherapeutic approach (5,6). Recent guidelines for the treatment of BPD highlight the central role of the disorder-specific psychotherapeutic interventions in the management of this disorder (7-10).

To date, models of psychotherapy that were more widely studied in BPD as single or combined treatments are: dialectical behavior therapy (DBT) (11-13), mentalization-based treatment (MBT) (14), transference-focused psychotherapy (TFP) (15,16), cognitive therapy (CT) (17), schema-focused therapy (SFT) (18,19), and system training for emotional predictability and problem solving (STEPPS) (20). In more recent years, interpersonal psychotherapy adapted to BPD patients (IPT-BPD) was introduced as a tailored intervention for BPD in addition to the other specific models of psychotherapy (21-25). IPT adapted for BPD has its roots in the traditional IPT for major depression (26). IPT-BPD was outlined by Markowitz (21) in order to address the essential features of BPD and to relieve the interpersonal troubles typical of these patients. In recent years, we proposed a revision of the IPT-BPD: IPT-BPD-R lasting 10 months (27).

If, on the one hand, the clinical effects of available treatments for BPD were largely investigated, on the other hand how the improvement of symptoms translates into changes in cerebral functioning of specific areas is yet to be established. In the past years, initial studies of neuroimaging have suggested that BPD treatments entail at brain level to obtain a therapeutic effect (28). For example,

dialectical behavior therapy seems to modulate neural underpinnings of emotion regulation, while transference focused psychotherapy seems to downregulate neural circuits of impulsivity (29-36). Taken together, available findings suggest that disorder-specific psychotherapies may modulate brain functioning throughout the downregulation of brain activity in the limbic regions, in particular insula and amygdala, and with the differential recruitment of prefrontal areas, mainly anterior cingulate cortex (ACC), orbitofrontal cortex, and dorsolateral prefrontal cortex (DLPFC), as well as enhanced functional connectivity between limbic and prefrontal regions (37,38).

To date, no studies have investigated the potential effects of IPT on brain activities in patients with BPD.

Our research group, has performed a previous fMRI study with the objective to evaluate the differences in brain functioning of BPD patients versus healthy controls during a task of autobiographical memory with the exposure to resolved and unresolved life events (39).

Results showed significant differences between the two groups in unresolved life events concerning the activity of the anterior cingulate cortex (ACC), the dorsolateral prefrontal cortex (DLPFC), and the temporo-parietal junction (TPJ).

The present fMRI study is aimed to evaluate, in the BPD group, changes of brain activity in patients who received IPT-BPD-R for 10 months versus patients who were in waiting list (WL) in the same period.

2. Materials and Methods

2.1 Participants

For this pre-post study participants received a diagnosis of BPD according with DSM-5 criteria (40). A part of them (N = 24) were included in a previous fMRI study (39). Patients were recruited at the Center for Personality Disorders - Department of Neuroscience, University of Turin, Italy. As in the previous study the exclusion criteria in the patient pool were: delirium, cognitive and

neurological diseases; schizophrenia and other psychotic disorders; bipolar disorders; concomitant major depressive episode; post-traumatic stress disorder; substance use disorder. Female patients of childbearing age were excluded if they were not using adequate birth control methods (according to the judgment of clinicians).

All participants (43 BPD patients) were assigned in a random way to two independent groups: subjects receiving IPT-BPD-R (N = 22 patients) and patients in waiting list (WL) with clinical management (N = 21 patients). Participants did not receive medications for the duration of the trial. Occasional assumption of benzodiazepines (lorazepam up to 2,5 mg/day; alprazolam up to 1mg/day) and hypnotic (zolpidem up to 10 mg/day) were allowed in both groups up to a week before the fMRI. Patients enrolled were outpatients that were not hospitalized during the study.

The 22 patients who received IPT-BPD-R and the 21 patients who were in WL were matched for gender, age, and education (number of years completed at school and university referred by patients and confirmed by school and academic certificates). All participants had right handed dominance with range for right handedness Laterality Index (LI) $48 \leq LI < 100$ (40) and they were aged between 18 and 60 years and. Males and females were included in both groups.

Two therapists who were trained for IPT-BPD with at least two supervised cases and with 5 years of experience provided psychotherapy. Sessions of psychotherapy were steadily supervised by a senior psychotherapist (S.B.) who checked for the observance of the manual. Clinical visits were also monitored to ensure that interpersonal dysfunctions of patients were not focused on. Treatment costs were covered by the Italian Health Service.

Each patient voluntarily participated in the study, after providing written informed consent. We observed the Declaration of Helsinki guidelines. Approval was obtained from the ethics committee of the University Hospital “Città della Salute e della Scienza –Ospedale dell’Ordine Mauriziano” of Turin. The trial was registered in the Australian New Zealand Clinical Trials Registry (ANZCTR) and allocated the code: ACTRN12619000078156.

2.2 Clinical measures

Both groups (patients in IPT-BPD-R and patients in WL) were tested by an expert clinician trained in assessment instruments (P.B.) before and after the period of treatment or WL with the following evaluation instruments: the Social and Occupational Functioning Assessment Scale (42); the Clinical Global Impression Scale, Severity item (CGI-S) (43), the Borderline Personality Disorder Severity Index (BPDSI) (44), the Barratt Impulsiveness Scale, version 11 (BIS-11) (45). In order to obtain the life events for the fMRI task, all patients were assessed with the Autobiographical Interview (AI) (46).

The SOFAS is a clinician-rated scale to measure a patient's impairment in social and occupational areas. It is independent of the psychiatric diagnosis and the severity of the patient's symptoms. The score is ranged between 0 and 100. Higher scores indicate a better functioning.

The BPDSI is a semi-structured clinical interview assessing frequency and severity of BPD related symptoms. The interview consists of eight items scored on a 10-point frequency scale (0 = never; 10 = daily), including ‘abandonment’, ‘inter-personal relationships’, ‘impulsivity’, ‘para-suicidal behavior’, ‘affective instability’, ‘emptiness’, ‘outbursts of anger’, ‘dissociation and paranoid ideation’, and of one item scored on a four-point severity scale, concerning ‘identity’. The BPDSI showed adequate reliability and construct validity.

The BIS-11 is a 30-items self-report questionnaire measuring the trait of impulsivity on a 4-point Likert scale. Higher scores for each item indicate higher levels of impulsivity. Twelve items are reverse-scored, in order to avoid response sets. Is it possible to identify three factors: cognitive impulsivity, motor impulsivity, and non-planning impulsivity. Global score is obtained by the sum of these factors. The BIS-11 showed adequate reliability and construct validity in both and Italian samples.

The Autobiographical Interview (AI) covered lifespan including interpersonal relationships with significant others. It is designed to obtain 2 unresolved life events (one with a positive and one with

a negative content) and 2 resolved life events (one with a positive and one with a negative content). Subject together with the clinician selected the significant life events. Subject listed for each life event 4 keywords, that were used to trigger active recall during fMRI. Moreover, the clinician prepared at the end of the interview a brief summary (number of words between 25 and 27) for each event. Four brief summaries and 16 keywords were collected for each subject from AI to present the unresolved versus resolved life events during fMRI. We considered as resolved event a life experience that the subject conceived as totally elaborated and concluded, while we considered as unresolved event a life experience that still produced its effects on the present and that the subject conceived as not completely integrated in his inner narration (39).

In addition, before performing fMRI all subjects identified 4 neutral stories (number of words between 25 and 27), with 4 keywords for event. Summaries are only used to contextualize the event. So, they provide information that concern the context of all the four keywords. The keywords indicate the meaning to the event: resolved, unresolved and neutral. Events and keywords with a neutral meaning were chosen among a pre-established set of neutral brief stories. Particular attention was payed to be sure that neutral stories did not include social content and interpersonal interactions. A preliminary set of neutral stories (44) was previously administered to 130 subjects, who indicated which stories and keywords they considered as neutral. Only stories that were found neutral by > 80% of subjects were used in the task as control conditions (21 stories). Neutral stories did not concern autobiographical event.

Before the fMRI participants were asked to check and confirm that each event was correctly allocated among resolved or unresolved experiences.

2.3 Interpersonal psychotherapy adapted for BPD - Revised

IPT-BPD-R consists of 10 months of therapy divided into two phases of 22 sessions and 20 sessions. The duration of sessions is 50 minutes. In the first phase (22 sessions) the objectives of therapy are to establish the therapeutic alliance, limit the self-destructive behaviors, and provide an

initial symptoms relief. Continuation phase (20 sessions) is aimed at maintaining a strong therapeutic alliance, treating distorted interpersonal dynamics, and developing more adaptive skills. Three additional sessions can be provided at the end of the 42 sessions if patients show serious difficulties during the termination phase. In situations of crisis, the therapist allows the patient two weekly contacts of 10' by phone. If needed hospitalization for a brief period of 7-10 days can be considered. During the hospitalization IPT-BPD-R continues when the patient's clinical conditions allow it. In our revised model of IPT-BPD is also included an intervention for patients' family members in order to help them to cope with the illness of their relative (27). In this study were included only outpatients who were not admitted to hospital during the intervention.

2.4 Waiting list

BPD patients who did not receive psychotherapy were monitored with weekly clinical visits lasting 50 minutes. Symptoms reported by the patient were taken into account and managed with a supportive approach.

2.5 fMRI task

Both groups underwent a pre-treatment fMRI run and a post-treatment fMRI run. Approximately 10 months elapsed between the first and the second run. During each fMRI experimental session we applied the task used in our previous study (39) that intercepts hemodynamic response in the brain regions of interest during the presentation of two types of events, resolved and unresolved. Each patient was instructed to recall resolved or unresolved content related to each life event. fMRI task included a control condition consisting of neutral events. Before each pre- and post-treatment fMRI experimental sessions, all patients were administered a training session in which we used a set of life events different from those of the experimental sessions.

We used the same experimental procedure of our previous study for both pre- and post-treatment fMRI runs (39). The same stimuli and fMRI task were presented to each patient during the two

fMRI scans. The task was created using E-Prime software to show the visual stimuli consisting of the text of events for the conditions: resolved, unresolved, and neutral (Psychology Software Tools, Inc., Pittsburgh, PA). The display system was supported by the specific glasses (Philips Resonance Technology, Inc.). The fMRI task (39) consisted of 24 trials divided into 3 type of conditions: 8 resolved, 8 unresolved, and 8 neutral. All trials were pseudorandomized for each patient.

They have been organized in the following order: 1) summary (duration = 15 s) - brief summary of the life event; 2) fixation cross (duration = 5/6 s); 3) keyword (duration = 5 s); 4) fixation cross (duration = 6/7 s) ; 5) response screen (duration = 4s), during which all patients were asked to identify the experienced emotion using three possible responses: “positive”, or “neutral”, or “negative”. The last phase was used to control that the task was performed in a correct manner (for more details see our previous study - 39).

fMRI Data Acquisition

All RM images were acquired for pre- and post-treatment fMRI experimental sessions at the Center of Brain Imaging 3T-NIT - Hospital Città della Salute e della Scienza, Turin, Italy with a 3.0 T MRI Scanner (Philips Ingenia) equipped with a 32 channel array head coil. For each pre- and post-treatment fMRI experimental session, functional and structural images were recorded. For the acquisition of functional images we applied an Echo-Planar Image sequence (EPI) with the following parameters: TR/TE = 3000/30 ms, 415 volumes, 32 slices, matrix size = 92×96, field of view (FOV) = 224 × 224 mm^2, slice gap = 0.5 mm, slices aligned on the AC-PC line, flip angle = 90°. For the acquisition of structural images we applied a T1-weighted sequence with the following parameters: TR 8.1 ms, voxel size 1 × 1 × 1 mm^3, TI 900 ms, TE 3.7 ms.

fMRI analysis

We analyzed all functional and structural images using Statistical Parametric Mapping 12 software (SPM12, Wellcome Department of Cognitive Neurology, London, UK) (47) interfaced on Matlab (Mathworks, Cherborn, MA, USA).

For each pre- and post-treatment fMRI experimental session, all images were pre-processed in line with our previous study (for details about pre-processing procedure for realignment, co-registration, segmentation, and normalisation see previous study-38). After pre-processing, for pre- and post-treatment fMRI runs of each patient we performed the General Linear Model (GLM).

At first level, we convolved in the design matrix a stick function with a hemodynamic response function (HRF) to regressors of interest modelled in 3 contrasts: resolved keyword, unresolved keyword, neutral keyword. In order to use a rigorous quality control check we defined six parametric regressors of no interest to correct residual effects of head motion and we excluded motion artefacts using the threshold > 2 mm translation and 2-degree rotation.

At the second level, in order to investigate how interpersonal psychotherapy modulates brain areas in BPD patients, we compared the two groups in IPT-BPD-R and in waiting list for post-treatment fMRI run *vs* pre-treatment fMRI run using a full-factorial design, with the factor treatment group as independent between-subjects factor, the factor life-event at three levels (resolved keyword, unresolved keyword, neutral keyword) and the factor time (before and after treatment) as within subjects factor.

We preliminarily computed the whole-brain exploratory analysis with a threshold of $p < 0.05$ FWE-corrected threshold.

Our a priori hypotheses were based on results of the previous study (39). For this reason we performed SVC-based analyses using a small volume correction (SVC) on the following coordinates centered with spheres of 10 mm radius: right Anterior Cingulate Cortex (rACC, x = 8, y = 39, z = 12); left Anterior Cingulate Cortex (lACC, x = -10, y = 29, z = 12); right Dorsolateral Prefrontal Cortex (rDLPFC, x= 41, y = 17, z = 30); left Dorsolateral Prefrontal Cortex (lDLPFC, x

= -37, y = 19, z = 26); right Temporal Parietal Junction (rTPJ, x = 42, y = -56, z = 34). In addition, we computed the correlation between decrease of brain activity and improvement of BPD symptoms (decrease of BPDSI total score after treatment) for the contrast between unresolved condition and neutral condition in each group. Spearman's Rank non-parametric (i.e. Spearman ρ) correlations were calculated. In particular, we extracted contrast estimates at the first-level and correlated these scores with BPDSI total score, applying the toolbox REX (http://web.mit.edu/swg/software.htm).

3. Results

3.1 Sample characteristics

The two groups in IPT-BPD-R (N = 22) and in WL/CM (N = 21) were analyzed at baseline with t-test and chi-square test to compare age, gendere distribution, and level of education. Results did not show any significant difference between groups (Table 1).

Analysis of variance was calculated between the two groups at baseline to compare the four clinical rating scales: CGI-S, BIS-11, BPDSI, and SOFAS. Also this analysis did not find any significant difference (Table 2).

Three cases in the group treated with IPT-BPD-R (13.63%) and four cases in the group in WL/CM (19.05%) dropped-out in the first month of the trial due to lack of adherence to study protocol.

3.2 Treatment outcome

Treatment outcome was assessed in the whole sample of 43 BPD patients with the intention to treat – last observation carried forward (ITT-LOCF) analysis. So, also the 7 patients who dropped-out were considered. Results of the ANOVA for repeated measures performed in BPD patients treated with IPT-BPD-R versus BPD patients in waiting list showed a significant improvement (within-subjects effect) with respect for the four clinical rating scales. In particular, a significant decrease was found for CGI-S ($P = 0.039$), BPDSI ($P = 0.001$), and BIS-11($P = 0.001$), while SOFAS score

showed a significant increase (P = 0.03). In addition, a significant between-subjects effect was found for the four scales in favor of the IPT-BPD-R treated group (CGI-S: P = 0.011; BPDSI: P = 0.009; BIS-11: P = 0.033; SOFAS: P = 0.022). Results are reported in detail in Table 3.

Patients included in this fMRI study were the same already assessed in a study of clinical response (48).

fMRI results

We report the following results about t-contrasts of interest for keywords analysed for the differences between the IPT-BPD-R group versus the group in waiting list.

Post versus Pre: Unresolved life event condition versus neutral condition

The SVC-based analyses showed a significant decrease of activity in the right Temporal Parietal Junction (rTPJ, x = 45, y = -51, z = 36) and in the right Anterior Cingulate Cortex (rACC, x = -4, y = 37, z = 8) (Figure 1 and Table 1).

In addition, we analysed the correlation between the change of activity of rTPJ and rACC the and decrease of BPDSI total score for the contrast between unresolved condition and neutral condition in each group. In the IPT-BPD-R group, the change of activity of the two regions was significantly correlated with the decrease of BPDSI total score (rTPJ: $\rho = 0.38$; $p = 0.022$; rACC: $\rho = 0.41$; $p = 0.016$). No brain region showed a significant correlation with BPDSI total score in the WL/CM group.

Please insert here the Figure 1

Figure 1. The comparison between the IPT-BPD-R group and the group in waiting list for post-treatment fMRI run versus pre-treatment fMRI run for the contrast unresolved condition versus neutral condition. Statistical maps are displayed on a standard T1 template using the MRIcron software package (48) with a threshold of $p < 0.001$ uncorrected for illustrative purposes.

Table 4. Contrasts of interest

IPT-BPD-R group > waiting list condition group for Post > Pre

	MNI Coordinates			Z-score	T-value	P-value
Anatomical Region	*X*	*Y*	*Z*			
Unresolved condition > neutral condition						
Right Temporal Parietal Junction	45	-51	36	3.22	3.40	.043
Right Anterior Cingulate Cortex	-4	37	8	4.13	4.56	.021

Significant voxels are reported threshold of $p< 0.05$ corrected. Peak activity coordinates are reported in MNI space.

All contrasts were computed using small volume correction (SVC) with a sphere of 10 mm radius and a statistical threshold of $p < .05$ family-wise error corrected for multiple comparisons at the voxel level over small volumes of interest.

4. Discussion

This is the first neuroimaging study that was aimed to investigate therapy induced changes of brain functioning in patients with borderline personality disorder who received Interpersonal Psychotherapy adapted to BPD in comparison with patients in waiting list. In the light of available evidence, it was hypothesized that BPD patients who receive psychotherapy show a modulation in neural activity patterns compared to untreated subjects. The hypothesis was confirmed by our findings, evidencing significant differences in the activity of specific brain areas after interpersonal psychotherapy. Patients were exposed during fMRI to unresolved, resolved life events and neutral

stimuli. In particular, significant pre-post differences in brain functioning concerned the right anterior cingulate cortex and the right temporal-parietal junction, during the exposure to the unresolved events obtained with Autobiographical Interview versus neutral stimuli. On the other hand, no significant changes in brain functioning were observed after interpersonal psychotherapy during the exposure to the resolved events versus neutral stimuli.

These results suggested that the efficacy of IPT-BPD-R on BPD symptoms may be underpinned by functional changes in brain areas involved in self-referential processing, social cognition, and mentalization (31,38,50-52). IPT-DBP-R may contribute to increase awareness of one's emotions and to discriminate self-emotions from those of the others, improve the mobilization of cognitive and emotional resources necessary to face interpersonal distress, modulate affective states in interpersonal contexts reducing hypersensitivity to rejection, alleviating feelings of abandonment and improving trust towards others (52).

Changes in brain functioning are associated with the clinical effects of psychotherapy. Thus, the improvement with IPT-BPD-R in severity of borderline symptoms may be observed also in terms of brain activity modulation between pre- and post- treatment.

Unfortunately, the comparison with previous studies on this field is hampered by the fact that this is the first trial that specifically investigated the effect of IPT-BPD-R on brain activity. It is only to compare our findings with trials that evaluated cerebral functioning before and after other interventions of psychotherapy for BPD, such as DBT and TFP.

Decrease in ACC activity after psychotherapy is consistent with the majority of available data, obtained in studies of DBT (29,31,32,35) and TFP (34). There is a general consensus among trials that the anterior cingulate cortex can be considered a target for the action of psychotherapy, as it is involved in the mechanisms that allow individuals to orient not only in their own mental state, but also in the mental states of others (53,54). Modulation of ACC after IPT-BPD-R during the recall of unresolved life events may underlie the effects on affective states and impulsivity in patients who were treated with a specific psychotherapy for BPD.

In contrast to ACC, previous data of brain imaging studies about the effect of psychotherapy on the activity of TPJ are not available. However, several previous studies identified TPJ as the main neural structure involved in processes of mentalization (55) and evaluation of emotional states in social situations (56-59).

Our findings indicated that BPD patients treated with IPT-BPD-R showed a significant decrease in activity of right TPJ when they were exposed during fMRI to unresolved life-events. A possible explanation is that psychotherapy produces an improvement of BPD symptoms, including impulsivity, with positive consequences on their self-awareness, consciousness and social cognition. In particular, the assumption of BPD patients, that "others will reject them", is attenuated (52). Improvement of their interpersonal exchanges and social inclusion allows patients to face with more adequate strategies unresolved life-events. These clinical and behavioral effects matched with the modulation of brain activity in structures with a key role in the theory of mind network (60).

The main strength of this trial is that it is the first evaluation of the effects of interpersonal psychotherapy for BPD (IPT-DBT-R) on brain activity of patients during an fMRI task.

The study suffers from some limitations. The first limit depends on the exclusion of comorbid psychiatric disorders in order to obtain a sample with more homogeneous clinical characteristics and to avoid the effects of comorbidity on treatment response. The negative effect of this exclusion is that this sample is not fully representative of the clinical population of BPD patients, commonly characterized by high rates of psychiatric comorbidity. Another limitation concerns the fMRI task, that consists in the exposure of subjects to unresolved and resolved life events identified with the Autobiographical Interview. BPD patients typically present an unstable sense of self and the tendency to change their opinion regarding significant life events, whether they are resolved or not during the time. In order to reduce the effect of this limitation, participants have re-examined the summaries of life events immediately before the fMRI scans to confirm that each event had been correctly assigned to the resolved or unsolved experiences. Finally, this study did not use a non-

patient control group and a responder analysis to examine differences between patients who responded and those who did not respond to psychotherapy was not performed.

Our initial findings suggested that this specific intervention of psychotherapy is effective in treating BPD symptom and that clinical effects are reflected in functional changes observed with neuroimaging techniques. Brain areas that showed a decrease of their activity are key structures of the network of theory of mind that are fundamental in BPD pathology. It would be of interest not only to replicate these findings, but also to conduct long-term evaluations that can explore potential delayed effects of interpersonal psychotherapy on the function of these areas.

Clinical points

1. Therapy of borderline personality disorder is a challenge for clinicians. Interpersonal Psychotherapy adapted for BPD (IPT-BPD-R) is a manualized treatment focused on interpersonal problems and aimed to improve specific BPD symptoms.

2. Findings of the present study suggest the efficacy of IPT-BPD-R as single treatment of BPD patients.

2. Our data indicate that IPT-BPD-R modulate the activity of brain areas involved in the network of theory of mind and mentalization processes.

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